ARMORED MEDICAL RESEARCH LABORATORY
Fort Knox, Kentucky

Project No. 50
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STUDY OF MEN DRINKING BURSOLINE TREATED
WATER IN MOIST HEAT

1. PROJECT NO. 50 - Final Report on the Physiological Effects of Ingestion of Large Quantities of Bursoline Treated Water.

a. Authority - First Memo Indorsement SPMDO, ASF SGO, dated 10 November 1944 to Memorandum dated 30 October 1944, Director Technical Division, SGO to Director Occupational Health Division, SGO.

b. Purpose - To study the behavior and performance of military personnel when drinking large quantities of water treated with Bursoline while working in high temperatures and humidities; to study the effect of Bursoline on the basal metabolism; and to determine the fate of the ingested iodine.

2. DISCUSSION:

a. Bursoline is an iodine preparation which has been recommended for use by troops in the field for individual sterilization of water. This agent has been shown to act more rapidly and to constitute a more effective cysticidal agent than chlorine preparations. The specifications call for 8.2 mgm. free iodine and 8.2 mgm. iodine combined in diglycine hydriodide in each tablet (see Sanitary Engineering Report No. 4, CMR of OSRD entitled, "Summary Report of the Effectiveness of Bursoline #3 Tablets in the Disinfection of Water in Canteens," dated 1 July 1944).

b. In the present experiments, 14 men lived and worked in the simulated jungle environment of a laboratory hot room for 45 days. For 38 days 10 men, group B, consumed water treated with Bursoline in a concentration equivalent to 2 tablets per quart. The remaining 4 men, group A, formed a control group and drank salted Fort Knox tap water. During the last 6 days the groups were reversed and group A drank Bursoline treated water and group B untreated water. All men marched 5 hours daily in a severely hot humid environment. This necessitated the ingestion of large quantities of water and provided a more rigorous test of the general physiological effect of Bursoline than would ordinarily be encountered in the field. The small number of men involved, prevented any evaluation of the incidence or importance of iodine sensitivity.

3. CONCLUSIONS:

a. Bursoline in quantities of up to 20 tablets per working day was consumed by the subjects without complaint as to taste or appearance of the treated water.

b. There was no evidence of any ill effect produced by drinking Bursoline treated water upon the subjects working in a hot humid environment under the circumstances of this test.

c. The iodine ingested with the treated water was rapidly eliminated by the subjects. Three to five days after stopping Bursoline, plasma and urine iodine had fallen to very low levels.

4. RECOMMENDATIONS:

That the results of these tests be distributed to agencies responsible for Army water purification procedures.

5. NOTE:

The conditions and limited magnitude of the tests herein reported permit no conclusions as to the importance of iodine sensitivity among troops ingesting Bursoline treated water. Questions relative to prevalence of iodine sensitivity, whether or not drinking Bursoline treated water induces or increases the severity of iodine sensitivity, and the extent to which the incidence of such sensitivity might offset the stated advantages of Bursoline for water purification, can be answered only in field tests of adequate magnitude.

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APPENDIX I

EXPERIMENTAL CONDITIONS AND PROCEDURES

1. Plan of Test:

The purpose of the test was to observe the effect of ingestion of large quantities of Bursoline treated water on the health of a group of young men. Thirteen men were closely observed for 45 days, living and working in the controlled heat and humidity of a laboratory hot room. The subjects were divided into two groups, A and B, drinking Bursoline treated water and living in moist heat, as outlined below.

SCHEDULE OF EXPOSURE TO BURSOLINE AND TO MOIST HEAT

GROUP	Cool Control Period 6 Days Days -6 thru -1	Period of Moist Heat 38 Days Days 1 thru 38	1 Day Day 39	6 Days Days 40 thru 45	Cool Control Period 3 Days Days 46 thru 48
A	T	S	S	B	T
B	T	B	S	S	T

T = Tap water, untreated
S = Tap water, salted to 0.1%
B = Bursoline treated, chlorine-free water, salted to 0.1%

2. Environment:

The test environment selected demanded a high water intake during the five hours of work performed each day. Between 0800 and 1630 hours the dry bulb temperature was kept between 91° and 92°F and the relative humidity at 95%.* Generally the temperature variations around the desired temperature did not exceed 1.0°F but occasionally greater fluctuations occurred. Regulation was most difficult at the start of the work day when the surfaces of the room and the ambient air had not reached equilibrium.

At 1630 hours the men left the room for approximately 30 minutes and the room was partially dried and cooled to approximately 82°F dry bulb temperature.

* During the 2nd 3 day period the dry bulb temperature was reduced about 1°F because of the large number of minor casualties.

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This temperature was maintained until 0800 the following day, with relative humidities varying between 30% and 50%. Fairly large fluctuations in temperature occurred in this period. The men remained in the room at all times except for a 30 minute period at 1630 and approximately 10 minutes at 0745, at which times they were exposed to the laboratory atmosphere of approximately 70°F dry bulb temperature.*

3. Experimental Subjects:

Fourteen enlisted men from a tank destroyer battalion served as subjects. They were divided into two groups—group A of 3** men and group B of 10 men. In making the separation, comparability as to age, body build, home state, average heart rate, rectal temperature and sweating rates after work in the cool environment were taken into account (see Table 1). Differences in average water intake and urine output appeared during the exposure in the hot environment.

4. Clothing:

All men used previously worn 2-piece herringbone twill fatigue uniforms during work periods. Clean dry uniforms and socks were provided at the start of each morning and afternoon work period in the heat. When not working, the subjects ordinarily wore only shorts. Standard service shoes were usually worn, but at times, jungle boots were used.

5. Preliminary Training:

The subjects had all been in the Army for 22 months, and had been taking regular exercise with some marches. During the week before the start of work in the heat the men marched from 1 to 3 hours each morning and afternoon. Some of this marching was done in the experimental room and observations of the type carried out later in the heat were made in order to familiarize the subjects with procedures, and to obtain control data.

6. Activity in the Hot Environment:

All men performed the same work of moderate intensity and long duration, walking single file around the room at a rate between 2.7 and 2.9 miles per hour, carrying a 20 pound pack. Unless incapacitated the men marched 3 hours in the morning and 2 hours in the afternoon. When special procedures were carried out early in the morning, the schedule was reversed and the walk lasted 2 hours in the morning and 3 hours in the afternoon. Data were always obtained at the start and

* Toward the close of the experiment men were occasionally out of the room for several hours in the evening but were never exposed to temperatures below 65-70°F.

** One subject from the original group of 4 dropped out after 4½ weeks in the hot room and has been omitted from the averages. His loss from the control group resulted in differences in average pulse and rectal temperature owing to the smallness of the group. These were not considered of significance in interpretation of the results.

finish of the work periods, and at times heart rates and rectal temperature were obtained at hourly intervals. No work was done on Sundays, and the high temperature and humidity were reduced Sunday afternoon to the night ranges.

7. Food:

Regular garrison rations were supplied from the company mess. The salt used for both cooking and seasoning was iodine free.

8. Water and Bursoline:

Non-iodized salt was added to all water to a concentration of 0.1%. Group A drank salted tap water (without Bursoline) for the first period of 39 days in the hot room, and Bursoline treated, unchlorinated water during the last 6 days in the hot environment. Men in group B drank Bursoline treated water during the first 38 days, and salted water during the last 7 days. Unsalted tap water was used by all during the control periods at the start and at the end of the test.

The water for both groups was from the same source—this was the Post water plant which is chiefly supplied from well sources. A typical analysis is given in Table 2. Water for Bursoline treatment was secured at the plant before chlorination and transported to the laboratory in a 250 gallon trailer three times a week. Each day's water requirement was separately treated with Bursoline. The treated water stood in aluminum containers for approximately 20 hours and was then decanted into 5 gallon pyrex bottles from which it was dispensed to the subjects. Each batch was analyzed for total and free iodine just before use. The experience of the first 6 days of the experiment indicated that there was a moderate but undesirable degree of variation in the Bursoline tablets. Thereafter a preliminary analysis was made on each batch at the time of preparation, and appropriate adjustment was made to give a total iodine concentration of between 33 and 36 mgm/liter. (34.7 mgm/liter corresponds to the concentration given by 2 tablets per quart of water. The specified iodine content of a single tablet is 16.4 mgm.) The average total concentration for the entire study (45 days or batches) was 34.8 mgm/liter, with a maximum of 39.1 and a minimum of 31.5 mgm/liter. The free iodine concentration averaged 11.4 mgm/liter (32.7% of the total), ranging from 8.4 to 13.6 mgm/liter. The Bursoline used was the product designated Bursoline No. 3, produced by the Burnham Soluble Iodine Company, Auburndale, Massachusetts, Lot Nos. 589-1 and 589-4.

All water was dispensed from a container (shown in Fig. 1) to the subjects by a trained technician. The volume was measured and recorded on an appropriate form. The dispenser had an automatic overflow outlet and was adjusted to deliver exactly 400 ml. of water into the paper cup from which each subject drank. Each man had a separate cup which was marked clearly with his name and group. Since most of the water was drunk while the subjects were walking, there was inevitably some spilling, and upon occasions the subjects purposely let water drip on their chests while drinking. Such infractions of water discipline were kept as low as possible by the technicians and officer on duty in the room at all times during the work periods. During the last week of the test all subjects drank while standing still in front of a technician or officer.

Five hundred ml. of milk, coffee or fruit juice were permitted with each meal but the average amount of fluid, other than water, consumed was less than a liter per day.

9. <u>Sleep:</u>

The men slept on canvas cots. Eight hours of sleep were scheduled each night and the men often slept 45 minutes to one hour after lunch.

10. <u>Observations during and after work:</u>

a. General appearance - Observations were made on flushing, vigor, alertness, and general reaction of the subjects to work in the heat. Symptoms of headache, dizziness, palpitation, nausea, and gastrointestinal cramps were noted.

b. Heart rate - At the start and finish of each morning and afternoon work period, and often at hourly intervals during work, the pulse rate was counted with the subject erect (standing still before the walk and marking time during and after work).

c. Rectal temperatures - These were recorded at the same intervals as the pulse rate. Clinical rectal thermometers, checked for accuracy, were used.

d. Weight - At the beginning and end of each work period the subjects were weighed (to within 15 grams) after removing clothes and towelling off. Water intake and urine output were recorded for each period to permit estimation of the rate of sweating.

e. Additional observations - Other observations, including blood pressure measurements, sweat collections, etc., were made at various times during the experiment.

11. <u>General observations:</u>

Careful measurements of the neck were made before and after the period of exposure to heat and use of Bursoline treated water. The feet were inspected regularly and treatment of blisters, bruises and arch difficulties were effected promptly. The skin was inspected at regular intervals. Appropriate measures were taken to control prickly heat and fungus infections.

12. <u>Iodine Studies:</u>

a. Water control - Bursoline treated water was dispensed and recorded as noted above (Section 8).

b. Urine collection - Consecutive 24 hour collections of urine were made on each subject for iodine analysis. Before going to the latrine to defecate, each subject was instructed to empty his bladder into the collecting bottle. During the clean-up periods an enlisted man was on duty in the latrine. It is probable that in spite of these precautions some urine was lost. During the walk, all subjects voided into a graduated cylinder and the quantity of urine was recorded for calculating sweat loss.

c. Plasma iodine was determined on 10 to 20 ml. samples of whole blood obtained in the fasting state or 20-30 minutes following the end of the afternoon work period. The usual schedule included bleedings Monday morning and afternoon, Wednesday afternoon and Saturday morning and afternoon.

d. Sweat iodine collections from the entire body were made by using suits of dry clothing and dry towels to prevent dripping during an hour's walk, and from the arm by use of a full arm length rubber gauntlet.

e. Iodine determinations were made on consecutive 7 day collections of feces from 2 men.

f. Skin sensitivity to the local application of U.S.I. tincture of iodine was tested during the 4th, 5th, and 6th weeks of the test. No control test was done prior to the use of Bursoline by group B.

13. Basal Metabolism:

The basal metabolic rate of each subject was determined on 3 occasions in the preliminary control cool environment. During the subsequent 6-week period in humid heat, the rates were determined on 14 occasions, or approximately twice weekly. On return to the cool environment, 4 further determinations were made. All subjects were without food 12 hours before the tests were made. They were awakened 5-10 minutes before each determination after 7-8 hours of sleep. The tests were made in the experimental room kept at the night temperature of DBT 80-85°F and relative humidity of 30-50%. The metabolic apparatus was wheeled to each subject who, in the majority of cases, had not moved from his bed.

Two Sanborn Waterless and two Benedict-Roth metabolism testing machines were used. Each machine was calibrated prior to use and frequently tested for leaks during the 8 weeks of use. The average test period lasted 12 minutes and none was less than 8 minutes in duration. Duplicate determinations on test days usually could not be made because of limitations in time.

Results were calculated from the slope of the graphic record of oxygen consumption. Correction factors for temperature and barometric pressure were taken from a standard table; surface area was determined according to Dubois and corrected for changes in weight during the progress of the experiment. The rates were expressed in terms of per cent above or below Krogh's modification of the Aub-Dubois standards.

193 of a total of 286 determinations, or 68%, were accepted as reliable measurements. Tests were excluded for several reasons: (1) if the graphic slope was not straight, (2) if the respiratory pattern was abnormal or deviated markedly from the subject's usual pattern, (3) if the calculated rate showed a striking deviation from the usual results for a given subject despite an otherwise satisfactory respiratory record.* With a few exceptions, unsatisfactory determinations gave high metabolic rates. As the subjects became accustomed to the procedure, the incidence of poor tests decreased.

14. Details of the analytical procedures and collection of material for iodine analysis are given in Appendix 3.

* Not more than 2% of results were excluded on this basis.

APPENDIX II

RESULTS

1. Acclimatization and Performance:

It has been previously observed that working men when first exposed to a hot environment do not drink enough water to replace that lost as sweat. This was true in both group A and group B. During the periods of drinking salted water and later of drinking Bursoline treated water the intakes of group A were higher than those of group B. This appeared to be a characteristic of the group rather than an effect of Bursoline. Mild objection was raised to the taste of Bursoline treated water at the start of the test. At the end of the test, however, the subjects complained that water without Bursoline tasted flat.

In Chart 1 are given the group averages for final post-work heart rate, rectal temperature, and sweat loss per hour for work in the control periods and work in the heat. Data have been compressed into averages for three days and include morning and afternoon work periods. The most obvious difference in response of the groups to work in the heat is the tendency for group B to have a relatively high pulse rate and low rectal temperature and for group A to have a less rapid pulse rate and a higher rectal temperature. This difference results chiefly from the reaction of one subject in group A who had a very slow pulse rate and relatively high rectal temperature after work.* If he is omitted from the calculations the lines for group A and group B are much closer together. It is not considered that the differences between the groups has any relation to the ingestion of Bursoline since the differences are apparent in the control periods, and persist during the week when the groups reverse their Bursoline intake program.

The phenomena of acclimatization were the same in the two groups and showed no significant differences in any of the subjects. Flushing of the face, edema of the hands, and the depression of morale appeared upon first exposure to heat and decreased at about the same rate to virtually disappear in all subjects by the end of a week. It was not possible to distinguish the controls from those taking Bursoline by their complaints of subjective distress, their appearance and behavior, or by the alterations of heart rate and rectal temperature during the early stage of acclimatization or later in the progress of the test.

2. Morale:

The morale of all subjects was very low for the first few days. It improved slowly and was higher towards the end of the experiment. The type of incarceration and restraint necessary for proper control was very onerous, and confinement of 14 men in a small, unattractive room was naturally depressing. In the course of 8 weeks the subjects walked more than 600 miles around a 65 foot track shut up in a windowless room. Movies were shown three times weekly, and the radio or record player supplied forms of diversion which were only partially satisfactory. Nevertheless, no subject was lost to the experiment except for medical reasons.

* This type of response has been noted in a number of subjects: See AMRL Report on Project No. 2, dated 18 October 1943.

3. Skin:

There were the usual prickly heat and non-specific skin rashes. They were slightly more severe in the control group during their period on iodine-free water than they were in subjects ingesting Bursoline. There was no indication of iodism. One subject was found to be sensitive to iodine applied locally to a cut on the leg. Tests to determine iodine sensitivity were done during the 4th, 5th and 6th weeks, and this subject was the only one sensitive to iodine. He was aware of no previous sensitivity and had used no iodine on his skin for at least two years. It is not possible to say whether he acquired his sensitivity during the period of ingesting Bursoline or whether he had it at the start of the test.

4. Basal Metabolism:

The results of 193 tests accepted as reliable individual determinations are presented in Table 3. The average of results for group A, group B, and for both groups combined are graphically presented in Chart 2. No significant trend in metabolic rate can be observed either for individuals or for groups.

5. Weight Loss:

There was a slight loss of weight in most of the subjects during the test, averaging 0.83 Kg. for group A and 1.48 Kg. for group B. This has been the usual experience in this type of environmental exposure.

6. Thyroid Gland and Neck Size:

No changes occurred in the size or consistency of the thyroid gland in these subjects and there was no change in the circumference of the neck during or after ingestion of Bursoline by the subjects in either group A or group B.

7. Blood and Urine:

Routine blood and urine analyses were performed on samples taken in the preliminary cool control environment and again after 38 days of exposure to heat.

There was an average fall of 0.9 gm/100 ml. of hemoglobin in group B and 0.6 mg/100 ml. in group A. Such a fall has been noted in previous studies on men living in the laboratory hot room and therefore does not appear to be an effect of Bursoline. The white counts, differential counts, and smears showed no abnormalities except in one case. Subject Fie showed a total of 4,350 white blood cells per cu. mm. with 8% eosinophils in the control period and 4,120 white blood cells per cu. mm. with 14% eosinophils at the end of the Bursoline period. It was this subject who showed evidence of iodine sensitivity.

The urine analyses showed no albumin or sugar and were negative on microscopic examination except for one case. This subject (Bur) showed albumin and white blood cells before and after the test period, presumably resulting from a chronic infection of the G-U tract.

8. Amount of Bursoline Ingested:

In order to ensure a severe test, the experiment was designed to

provide iodine intake exceeding the highest levels likely to be found in military service. The Bursoline tablet contains sufficient active iodine to provide adequate sterilization of one quart of most waters. However, the necessity of treating water of high iodine demand is provided for in the directions for use of the tablets which read: "If the water contains rotten leaves, or is dirty and discolored, use 2 tablets" (per canteen). A table used in this laboratory as a rough guide to water requirements is reproduced below with the inclusion of the appropriate number of Bursoline tablets for the various situations. Comparison of this table with the amounts actually ingested in the present study (Chart 5) indicates that the Bursoline consumption reached the highest probable amounts for the most severe conditions likely to be encountered.

ILLUSTRATIVE DAILY WATER AND BURSOLINE REQUIREMENTS
FOR SEVERAL DEGREES OF WORK AND ENVIRONMENTAL STRESS

ACTIVITY	ILLUSTRATIVE DUTIES	MODERATE DESERT OR JUNGLE*	SEVERE DESERT OR JUNGLE**
Light	Desk work, guard and KP duty	6 quarts 6 or 12 tablets	10 quarts 10 or 20 tablets
Moderate	Route march on level, tank operations	7 quarts 7 or 14 tablets	11 quarts 11 or 22 tablets
Heavy	Forced marches, stevedoring, entrenching	9 quarts 9 or 18 tablets	13 quarts 13 or 26 tablets

* Desert: Air temperature below 105°F. Jungle: Air temperature below 85°F.

** Desert: Air temperature above 105°F. Jungle: Air temperature above 85°F.

From the standpoint of free iodine intake, the present study also represents an abnormal situation inasmuch as 2 tablets per quart would normally be used only where water of high iodine demand is used whereas the water employed in the present study had a negligible iodine demand. It is extremely unlikely that troops would ever be required to drink water having as high free iodine concentrations as that used here.

9. Chemical Studies:

a. General - The primary purpose of the rather extensive chemical studies in the present project was to provide background information which would permit correlation of blood levels with any observed symptoms or poor performance that might be ascribed to iodine. No evidence was found that iodine intake at the levels of the present study interfered with performance or produced symptoms. The chemical data stand therefore, as detached information on the levels obtained for given rates of intake which may be useful in evaluating subsequent experience with Bursoline. Also, although complete iodine balance studies were not done, it was possible to estimate the relative importance of the different paths of iodine elimination.

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Plasma rather than whole blood was chosen for analysis both because of the simplified technic of analysis (App. III) and the expectation that, since the distribution of the iodide ion is similar to that of chloride (1) the plasma should give a more stable index of iodine concentration than does whole blood. In addition, a protein free filtrate provides a homogenous source of iodide ion since the protein bound and organic iodine are removed with the protein precipitate (2) (3). The available evidence (3) indicates that ingestion of iodine or iodide primarily influences the ionic iodide fraction of plasma. Iodine present in body fluids is believed to exist exclusively in the reduced form. This is suggested both by the redox potential of these fluids and demonstration (4) that iodine is absorbed only after reduction to iodide. Unless iodine or iodides are being taken there is normally no ionic iodide in the plasma or at most only minute amounts (5), certainly less than 3 or 4 micrograms/100 ml. which is the lower limit of detection by the method of analysis used here.

Briefly the present studies indicated that the iodine in Bursoline treated water is rapidly absorbed, distributed, and excreted. Since the data from group A (3 men) were equivalent in every way to that from group B (10 men), the following discussion is chiefly limited to the results from group B. During the first 38 days of exposure to heat when group A was on salted tap water, the plasmas collected from the men in this group were uniformly negative for iodine (<10 micrograms/100 ml.); in four instances small amounts of iodine were found in the urine of these men (probably contamination) otherwise all were negative (< 0.1 mgm/liter).

b. Plasma Concentration of Iodine - The rapid rise and fall of plasma iodine is indicated by the curves shown on Chart 3. These plots show the plasma iodine concentration and iodine intake (Bursoline water = appproximately 35 mgm. iodine/liter) as functions of time. All of the curves show initial plasma levels which represent chiefly the iodine remaining from the previous day and to lesser extent the iodine intake during the night. With the onset of work, at about 0830 hours, rapid intake of water starts. By mid-morning the plasma iodine concentration has increased by several hundred micrograms per 100 ml., and rises still further with the continued intake during the remainder of the morning work period. The data from Subject 011, Chart 3 b, indicate that during the noon rest the slowed intake may lead to a slight fall in plasma level. The same pattern of continued rise follows the increased water intake during the afternoon work period leading to a peak level shortly after the high rate of intake falls with the completion of work. The plasma level then starts to fall and continues downward even though small amounts of iodine are consumed during the night. By the following morning, the level has fallen to about 40% (30 to 50%) of its peak value. The uniformity and rapidity of the disappearance of iodine from the plasma is indicated by Chart 4 where iodine level is plotted on a logarithmic scale against time. The linear plots in Chart 4 suggest that a uniform rate of disappearance (proportional to the concentration) prevails during the elimination of iodine. From the slope of the average line it is seen that if no more iodine is taken, plasma iodine concentration falls by 83% (to 17% of its initial value) in 24 hours. As will be shown later, the chief route of excretion is the urine.

The bleeding schedule adopted for the regularly scheduled bleedings was based on this rapidity of change and the weekly work pattern. This schedule called for sampling Monday at 0700, again Monday 20 to 30 minutes after the end of the afternoon work period, at the same interval after the afternoon work periods on

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Wednesday and Saturday, and at 0700 Saturday. This gave the minimum level of the week (Monday morning), the last morning level of the work week, and three peak values during the week. Both groups A and B were sampled according to the same pattern. Blood samples in each group were secured on each of the succeeding three mornings after Bursoline was stopped and at several later intervals from group B. The individual analyses of the bloods collected according to this schedule are collected in Table 4 and the averages for the groups in Chart 5. Chart 5, top panel, illustrates the characteristic weekly pattern of plasma iodine concentration which results from the work schedule. On Monday the level rapidly rises as the Bursoline intake increases with the increased sweat output of work. The peak levels reached at the end of each work day are maintained, or increase, in proportion to the water intake through the week and then fall abruptly over the rest day to a Monday minimum. The Saturday levels can be taken as representative of the normal diurnal change in concentration. In Chart 5, Saturday morning concentrations are connected by broken lines to the heavily lined envelope of maximum concentrations.

During the course of the experiment several factors combined to produce a gradual increase in the daily fluid intake; the work capacity improved, the sweating rate increased, and the environment became somewhat more severe as the study progressed. This increase in iodine intake is shown by the intake values in the center panel of Chart 5, and the reflection of this increase, in the gradual increase in peak plasma iodine levels. That this is not a result of a gradual accumulation in the plasma with continued intake is demonstrated by the low concentrations found in the Monday morning bleedings. These are all uniformly low and bear little relationship to the peak Saturday level. This is to be anticipated, for as indicated in Chart 4, not more than 5% of the concentration remains in the plasma after 48 hours of no intake. Consequently the Monday morning level is chiefly determined by the iodine taken in on Sunday. The rapidity with which the iodine is eliminated from the plasma after intake has stopped is apparent in Chart 5 as well as Chart 4 where the same data for group B are plotted on a semi-logarithmic grid. In group B, by the fourth day after stopping intake of iodine only one man had a plasma iodine concentration above 10 micrograms/100 ml.; in group A all were below this level by the third day after stopping intake.

The average peak plasma concentrations of group B were well above 1000 micrograms/100 ml. in the last weeks of the study. The highest level was above 1900 micrograms/100 ml. (Oli) and levels in excess of 1500 were not infrequent. As mentioned above, the plasma concentration gradually increased with increasing intake. The correlation between these is shown in Chart 6 where the average intake for the 6 working days of each full week of the study is plotted against the average plasma concentration of the three afternoon samples of each corresponding week. All of the men of group B are included. As indicated by the positions of the points for subject Fie, the lightest man in the group, and Fem, the heaviest, there is a correlation between body weight and the ratio of plasma level to intake. The correlation is, however, very low, and is striking only in the case of these two subjects who are at the extremes of their group.

c. Routes of Elimination - The chief route of elimination of iodine in these subjects was through the urine. As shown in the lower panel of Chart 5 (see also Table 5) about 75% of all the iodine given was recovered in the urine. An attempt was made to make short time measurements of the rate of iodine excretion in

the urine in order to define the characteristics of urine excretion as a function of plasma level and other factors. However, the tendency for all the subjects to lag behind their water requirements during the period of active sweating, which is also the period of high iodine level, and the consequent low rate of urine flow made accurately timed collections of urine very difficult. The available data indicate clearance rates of from 10 to 25 ml. plasma/min. with a tendency toward higher clearance rates with increasing urine flow; such clearance rates are consistent with the slopes of the plasma disappearacne lines in Chart 4.

Since an appreciable amount of iodine is required to produce iodine levels of 100 to 200 micrograms/100 ml.*, the temporary retention of this amount is apparent in the lag in urine excretion apparent in the first few days of Bursoline intake, as shown in Chart 5.

The sweat was of next importance in the elimination of iodine. Chart 7 and Tables 6 and 7 summarize the data on iodine concentration in sweat. In Chart 7, it is apparent that the sweat iodine is, to a degree, a function of the iodine concentration in plasma; roughly the sweat iodine concentration was 35% of the plasma iodine concentration. From Table 7 it can be seen that while the iodine concentration in arm sweat was of the same order of magnitude as the whole body sweat it was nevertheless uniformly higher in relation to the plasma level than whole body sweat by 25% to 30%. This may be due in part to regional differences in concentration. Data pertinent to the question of the analogy in sweat secretion between chloride and iodide was obtained in two experiments each on subjects Del and Bur. In two sweat collections on each man by the two technics (suit and sleeve) the ratios of sweat concentration to plasma concentration were; for the suit collections, iodine, 0.27 to 0.33, chloride, 0.35 to 0.40; and for the sleeve collections, iodine, 0.34 to 0.43, chloride, 0.30 to 0.43. This suggests considerable similarity in handling of the two halides by the sweat mechanism. The total output of iodine in the sweat was at times as much as 10% of intake (see Section d below).

Relative to the amount ingested, only minor amounts of iodine were found in the feces. Complete collections of one week made on subjects Ful and Tho led to recoveries of only 0.32% and 0.38% respectively for that week.

Attempts to develop a satisfactory procedure for collection of iodine in the expired air were not successful. However, it is believed that had significant amounts been present they would have been recovered.

d. Iodine Balance - A rigorously complete balance of iodine in the present study would have required complete collection of all sweat from the subjects, the use of pans for defecation both to collect the feces and to avoid urine loss at the time of defecation, and other similar precautions. The present data, necessarily

* A crude measure of this is given by the slope of the line in Chart 6. This indicates that on the average, about 30 mgm. of iodine are required for each 100 micrograms/100 ml. found in plasma. This is a somewhat larger amount than would be predicted on the basis that its volume of distribution would be equal to the extracellular fluid volume (1).

collected without the use of these refinements, nevertheless appear capable of supplying useful information on the probable disposition of iodine ingested as Bursoline.

The urine, which represents the chief path of elimination, accounts for a large part of the ingested iodine, despite the known incompleteness of collection. Of all the iodine given to group B in the 38 days that they received Bursoline, 74% was recovered in the urine (Table 5 and Chart 5). The same recovery of 74% was found in group A while on Bursoline treated water. In each case the amounts excreted beyond the third day after stopping Bursoline contributed insignificant quantities of iodine. In following the iodine excretion in the urine it was necessary to take into account several factors. For example, iodine which is initially retained is eventually recovered in the early days after stopping iodine intake. The effect of this is apparent in the cumulative recoveries shown in the bottom panel of Chart 5. Although the lag in excretion was short, it was sufficient to prevent useful calculation of a daily yield in the urine. Thus, on a rest day when the intake was low, there was invariably more excreted than taken in (center panel Chart 5). To obviate this cyclic irregularity, the device of calculating urine return in terms of a moving 7 day average was used; in this way each 7 day period included one rest day. The average 7 day yield is shown in the bottom panel of Chart 5 and for the individual subjects in successive 7 day periods in Table 5. It is apparent from the data on the 7 day yield in Chart 5, that a progressive increase in deficit occurred. This can be directly correlated with increased sweat output and undoubtedly reflects in some degree the increased loss of iodine in sweat at the higher sweat outputs.

With the information available on the urine, sweat, and feces it is possible to assemble a partial balance. This has been done in Table 8. The basis for calculation of the various components is as follows: fecal output was calculated as a percentage of the total intake (based on the results from subjects Tho and Ful of 0.38 and 0.32% respectively); sweat iodine output was calculated from the total sweat output, as estimated from the water intake less water output corrected for weight change, and an estimated iodine concentration in sweat derived from the correlation shown in Chart 7 (Sweat I = 0.35 Plasma I) where plasma I was taken as 0.77* x (average peak plasma concentration); the intake and urine output were taken from the sources already mentioned. The resulting balance, though obviously based on crude estimates, probably gives a fair picture of the relative contribution of the various paths of loss. When the deficiencies of the data are considered—the probable incompleteness of urine collection, the estimates in the case of sweat and feces, and the possibility that some spillage of Bursoline water may have occurred at the time of drinking—the suggestion is strong that retention was negligible. Note the data for subject Sce, for example, which show that all but 8.1% of ingested iodine was recovered.

* The factor 0.77 was derived from curves of the type shown in Chart 3 to approximate an integrated average concentration for the work periods—the period of high sweat output.

An added factor, already mentioned, which lends weight to the probability of negligible iodine retention is the great rapidity with which the plasma and urine become clear of iodine after intake is stopped. It seems unlikely that any significant amount of iodine was retained by these men.

10. Summary:

There was no indication that ingestion of large amounts of water treated with 2 tablets per quart of Bursoline had any deleterious effect on acclimatization, performance or metabolism under the circumstances of this experiment. The iodine ingested in the treated water was rapidly eliminated after Bursoline intake was stopped.

11. References are at the end of Appendix III.

APPENDIX III

ANALYTICAL PROCEDURES

1. Iodine Analysis:

a. General - The procedure finally adopted for the estimation of iodine in urine, sweat and protein-free filtrate of plasma was based on the oxidation of the iodine to iodate by permanganate. After reduction of the permanganate, iodide was added and the iodine liberated by the acid iodate was titrated with thiosulfate. In essence this is the Groak procedure (6) except that the permanganate serves for the destruction of residual interfering organic matter as well as iodine oxidation, and the reaction is carried out in an acid medium. Bromine rather than permanganate has been used in similar procedures for both plasma (7) and urine (8); the amount of iodine available for analysis in these procedures, however, was somewhat more than was available in the present studies. At the iodine levels encountered in the present study, 0.1 to 4 micrograms, the bromine oxidation of residual organic material was not sufficiently complete to avoid considerable end-point interference in the titration. The final procedure was well adapted to the handling of large numbers of analyses, and, in such routine use, was reliable to better than ± 0.1 microgram (see below).

b. Reagents -

H_3PO_4, 8 M - 1 volume 85% syrupy H_3PO_4, Merck, R.G., mixed with 1 volume distilled water.

$KMnO_4$, 1 N - Merck or Mallinckrodt U.S.P.

$NaNO_2$, 1 M - Merck, R.G.

Urea, 5 M - Merck U.S.P.

KI, 25% - Merck, R.G. Prepared daily with water thru which nitrogen had been bubbled for about ½ hour.

Starch, 1% - Merck soluble starch. Prepared fresh every 3 days.

Sodium Thiosulfate, 0.001 N - Prepared daily by dilution of standard 0.1 N Thiosulfate which was stored in the refrigerator.

c. Procedure - The method adopted was as follows: Appropriate aliquots of sweat, urine, or protein-free filtrates of plasma were measured into 125 ml. Erlenmeyer flasks and the volume made up to 20 ml. with distilled water. To these were added 0.25 ml. of 8 M H_3PO_4, 1 ml. of 1 N $KMnO_4$, and 2 glass beads to avoid bumping. The mixtures were brought to boiling over a battery of microburners. At the end of 10 minutes slow boiling, the flasks were removed from the flame. The sides were washed with water and 1 M $NaNO_2$ was added dropwise until the brown color and all specks of MnO_2 disappeared with mixing. An excess of 1 drop of $NaNO_2$ was added (total about 7 drops) and the walls of the flask again rinsed. Immediately

thereafter 4 drops of 5 M urea were added, the mixture was shaken and the flask returned to the flame. Oxidations were done in rotation by pairs, with 3 minutes elapsing between treatment of each pair. The contents of the flask were evaporated to about 5 ml. with vigorous boiling and stored in the refrigerator until titrated.

Titrations were carried out in the same flasks in which oxidation was performed. The flask was cooled in an ice bath, 0.125 ml. 25% KI and 3 drops 1% starch were added to the mixture immediately before titration. The liberated iodine was titrated to the nearest cubic millimeter with 0.001 N sodium thiosulfate delivered under the surface of the fluid from a Rehburg burette. The flask was replaced in the ice bath several times during the titration and was routinely cooled just before the end-point was reached.

Single analyses were performed on the material (plasma or urine) from subjects who were receiving no iodine. The largest permissible aliquots were used; these were 20 ml. of plasma filtrate and 0.2 ml. of urine. Positive results were checked with fresh material. All other analyses were carried out in duplicate, one aliquot being twice as large as the other. This provided a rigid control on the whole procedure.

d. Recoveries - A total of 35 determinations on known amounts of KI added to water and oxidized by the above procedure gave the recoveries shown in Table 9.

2. Plasma Preparation:

a. General - The barium hydroxide—zinc sulfate deproteinization procedure of Somogyi (9) was chosen for plasma treatment rather than his sodium hydroxide-zinc sulfate method, used by others (2) (3) (7) for iodine analyses, since the lower salt concentration obtained in the filtrate by the barium procedure leads to more favorable end-point conditions.

b. Reagents -

Potassium oxalate—purified by precipitation with alcohol from a saturated aqueous solution.

$ZnSO_4.6H_2O$, 5% wt./Vol.

$Ba(OH)_2$ approximately 0.3 N - The barium solution was adjusted so that 5 ml. zinc required between 4.7 and 4.8 ml. barium to produce a definite pink with phenolphthalein.

For oxidation, as above (Section 1).

c. Procedure - Blood was collected in test tubes on the sides of which potassium oxalate had been dried in sufficient amount to give 2.5 mgm/ml. of blood. Filtrates representing a 1-20 dilution of the plasma were prepared as follows: One volume of plasma was mixed with 17 volumes of water in a centrifuge tube. To this were added 1 volume of 0.3 N $Ba(OH)_2$ and, after mixing, 1 volume of 5% $ZnSO_4.6H_2O$. The whole was thoroughly mixed. The precipitate was separated by centrifugation, and the supernatant liquid filtered.

Suitable aliquots (5, 10 or 20 ml.) were oxidized and titrated as above (Section 1). Iodine concentration was calculated, using a factor which was based on the recoveries of known amounts of KI added to plasma filtrates.

d. Recoveries - Plasma from laboratory personnel was mixed with 1 volume per cent or less of a solution of a suitable concentration of KI in 0.9% saline and allowed to stand 20 minutes, after which it was treated as described above. The recoveries are shown in Table 9.

Recovery of iodine through the oxidation step was followed by analysis of plasma filtrates to which KI was added. The plasma filtrates used for this were prepared from the plasmas of subjects receiving no iodine. The filtrates were analyzed before iodine addition. The results are shown in Table 9.

3. Urine Preparation:

a. Procedure - Each day the urine for the preceding 24 hours was measured and a portion stored in the refrigerator until analyzed. For analysis, urines were suitably diluted with distilled water, 5 ml. urine to a final volume of 25 ml. for men drinking salted water and 0.5 ml. to 25 ml. for those drinking Bursoline water. Of these dilutions, 1.0 and 0.5 ml. were transferred to 125 ml. Erlenmeyer flasks. The volume was made up to 20 ml. with water and oxidation and titration carried out as described in Section 1.

b. Recoveries - The method was checked by oxidation of portions of a standard KI solution added to control urines, i.e. urines in which no iodine was demonstrated by the above procedure. Results are given in Table 9.

4. Sweat Preparation:

a. Suit collection - The suit was the same as that worn throughout the experiment except that a pair of wristlets was added to keep the bottom of the sleeves closed. The jacket was worn inside the trousers and the trouser legs were tucked inside the socks. The subject carried a towel to wipe off his face and hands, and the pack was enclosed in a waterproof sack. These precautions were taken to avoid sweat loss by dripping from the skin and suit, and to prevent contamination from sweat in the pack.

All of the clothing, including the towel was given a thorough washing before each use. This was carried out in a household washing machine and consisted of 5 treatments including rinses. Soap and calgonite were used on the first washing, calgonite alone on the second, and tap water on the last three. Each washing lasted 5 minutes and the clothing was put through the wringer after each washing. The clothing was dried, placed in a metal pan and brought into the hot room. After about 15 minutes for thermal equilibration the initial weight was taken.

All collections were made during work periods. The subject stopped walking, stripped, dried off with the towel he had been carrying, and was weighed. He then donned the tared clothing, picked up the tared towel and began walking. At the end of the walking period the subject stripped, replaced the clothing in the pan, and dried off with the tared towel, which was also replaced in the pan.

The subject and the pan plus clothing were weighed again. Final minus initial pan-plus-clothing-weight gave unevaporated sweat loss. Initial man-weight plus water intake during test minus urine excretion during test minus final man-weight gave total sweat loss. Time on test was taken from initial to final man-weight.

Sweat was extracted from the clothing with from 10 to 20 liters of tap water; 1 ml. 10% $NaHSO_3$ was added to each 10 liters of water to reduce the free chlorine, thus preventing the oxidation and subsequent volatilization of iodine. Extractions were carried out in large glass jars or in the washing machine. Ten minutes vigorous agitation was used in either case, and the clothes were run through the wringer of the washing machine at 5 and 10 minutes. After this treatment the distribution was considered adequate and an aliquot was taken for analysis. Extractions carried out in this way in both dry suits and suits worn by subjects not receiving iodine gave satisfactory recoveries of added iodide.

b. Sleeve collections - Collections of arm sweat were made in an arm length rubber-dam sleeve. The sleeve was in the form of an envelope cemented at the bottom and sides, and held in place from the top by a cord around the subject's neck. At the beginning of the collection, the subject's arm was bared, washed and dried, the sleeve put on, and walking begun. At the end of the collection period the sleeve was removed, the sweat being wiped off as well as possible by holding the top of the sleeve as tightly as practicable while the sleeve was slipped off. For some experiments the arm was finally dried with a tared towel, and the increase in bag and towel weight gave total loss of sweat. In other experiments the sweat was simply poured into a graduate and measured.

c. Analysis - Twenty and 10 ml. aliquots from the suit and 1.0 and 0.5 ml. aliquots from the sleeve collections were analyzed by the method given for plasma iodine determination (Section I). Sweat dilutions in suit collection were calculated from:

$$\frac{\text{Total Sweat Loss (Kg.)}}{\text{Vol. extracting liquid (l.)} + \text{unevaporated sweat loss (Kg.)}}$$

d. Fecal Iodine Determination:

The total fecal output of each of two subjects was collected for one week. Collections were started at the same time each day and each day's specimen was treated separately. The subject defecated into a tared aluminum mess can on the top of which a standard toilet seat was placed. Each day's output was weighed, transferred with a small amount of water to a Waring blendor, and homogenized with twice its weight of 2N-KOH. The blendor was rinsed with one additional weight of 2N-KOH. A few drops of caprylic alcohol were added during homogenization to prevent foaming. All the resulting suspensions were combined for the one week period. Analysis was carried out by the permanganate oxidation method of Riggs and Man (10).

6. Iodine Concentration in Bursoline Water:

The water mixed with Bursoline was originally dispensed in the hot room from aluminum containers. It was soon found that storage in the hot room in aluminum accelerated the reduction of free iodine to iodide (up to 20% reduction of free

iodine in 4 hours). After the 6th experimental day the water was decanted from the containers in which it was prepared and dispensed in the hot room from pyrex bottles.

The analysis of free iodine concentration in Bursoline water finally adopted was direct titration of iodine in the presence of H_2SO_4 and KI using 0.001 N $Na_2S_2O_3$. Approximately 1 gm. KI (measured with a glass scoop) was dissolved in 35 ml. Bursoline water by shaking. After the addition of 2.5 ml. 4 N H_2SO_4, the solution was titrated until the yellow color had almost disappeared. At this point, 3 drops of 1% starch were added and the titration finished.

Most of the earlier free iodine estimations were made without the addition of H_2SO_4. After 27 experimental days, the policy of adding H_2SO_4 was uniformly adopted. Concurrent analyses of water with and without the acid, showed a slight increase in free iodine determined in the presence of acid.

Total iodine concentration was determined on 20 ml. aliquots of Bursoline water. An aliquot in a 125 ml. Erlenmeyer flask was mixed with 0.02 ml. reagent bromine in the presence of 2 ml. 4 N H_2SO_4. The solution was boiled until the yellow color disappeared. Residual bromine was removed by the addition of 10 drops 10% sodium salicylate, and the sides of the flask washed with 10 ml. distilled water. The mixture was heated to boiling, removed from the flame, cooled to room temperature and, after the addition of 1 gm. KI, titrated with 0.002 N $Na_2S_2O_3$. Determinations of both total and free iodine were made in triplicate on each lot of Bursoline water.

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TABLE 1

CHARACTERISTICS OF GROUPS A AND B

	GROUP A 3 Subjects	GROUP B 10 Subjects
Age		
Average	20	20.4
Range	19 - 21	19 - 22
Average Weight (kg)	73.6	72.2
Average Height (inches)	68.7	70.0
Complexion & Hair Color		
Blond	1	3
Brunette	2	7
OBSERVATIONS AFTER STANDARD WALK IN COOL DBT 80°F, WBT 66°F		
Average Heart Rate	104	106
Average Rectal Temperature	99.9	99.9
Average Weight Loss per hour in grams	306	287

TABLE 1

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TABLE 2

TYPICAL ANALYSIS OF WATER FROM MULDRAUGH PLANT
FORT KNOX WATER SUPPLY SYSTEM

Office of the Post Engineer, Sanitary Department

Odor	Chlorine
pH	7-8
Pthn alkalinity	0.4
MO alkalinity	248
Soap consuming power	126
Total hardness	274
Dissolved oxygen	8-9
Oxygen consumed	0-1.0
Total solids	333
Suspended solids	0
Loss on ignition	96
Iron	0
Manganese	Trace
Aluminum	3.6
Silica	0
Calcium	58
Magnesium	29
Carbonates	0.8
Bicarbonates	247
Sulfates	41
Chlorides	7.7
Nitrites	0
Nitrates	0
Phosphates	0
Residual chlorine	0.3-0.6

TABLE 2

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TABLE 3

BASAL METABOLIC RATES (% NORMAL STANDARD)

DAY	-5,4*	-3	-2,1*	1	2	5	8	12	15	19	22	26	29	33	36	40	43	45	46	47	48
PERIOD	CONTROL			BURSOLINE + HEAT												HEAT		CONTROL			
Dev.	+1	-1			-5	+7	+8		-4		-5	-11	-15	+6	-14	-5	-1	-5	-4	-3	+1
Fie			0		+8		-6	-1	-1		-6	-9		+4	-4	-4		+3	+14	-11	-5
Kel		+4	+3	+8	+24	+4	+17	+17	+13	+16		+16	+13	+10	+16	+17		+17	+10		+16
Lue		-12	+7		-5	-8		+3		-4	-1	-12	-11	-15	-8		0	+9	-15		-2
Mag		+8			+8	-1	+5	+2	+4	-2	-8	+1	+7	-9	-11		-5	0	-2	-2	+4
Oli	+1				-17						-1	-1	-3	+10	-5		-15			+2	+10
Pem				+6							+6	+10		+11			-9	+5	+17		+1
Pul	-7	-15		-5	-5	-13	-5	-8	+1	-11	-16	-15	-2	-8	-14	-15	-15	-7	-15	-11	0
Sce			-2				-1	+3	-1	+2			-9							+4	
Tho		+1	0	-11		-15	-13		-10		-9	-17		-13	-6	-7	-3	+6	-7	-3	+2
AVG.	-1.7	-2.5	+1.6	-0.5	+1.1	-4.3	+0.7	+2.7	+0.3	+0.2	-5.0	-4.2	-2.9	-0.4	-5.8	-2.8	-7.0	+3.5	-0.3	-3.4	+3.0
PERIOD	CONTROL			HEAT ONLY												BURS. + H		CONTROL			
Thi		+6	+6	+5	+4	0	+5	+5	+8	+5	+4	+1	+10	+11	+14		+14		+9	+12	+12
Bur					-3	-1					-2		-6	+2	+11	+11	+6	-2	+6	+9	+7
Men	-1								-6		-11	-14	-10	-1	0						
Del	+3	-7	-6						+7	+13		-5	-8	-9	-3	-3	-6	-13	-5	-3	-5
AVG.	+1.0	-0.5	0.0	+5.0	+0.5	-0.5	+5.0	+5.0	+3.0	+9.0	-3.0	-6.0	-3.5	+0.8	+5.5	+4.0	+4.7	-7.5	+3.3	+6.0	+4.7
TOTAL AVG.	-0.6	-2.0	+1.1	+0.6	+1.0	-3.4	+1.3	+3.0	+1.1	+2.7	-4.5	-4.7	-3.1	0.0	-2.0	-0.9	-3.4	+1.3	+0.7	-0.6	+3.4

* # of Subjects tested on each day.

TABLE 4 SHEET 1

SUMMARY OF PLASMA IODINE CONCENTRATIONS

GROUP	SUBJECT NO.	BLEEDING NO		A	B	C	D	E	F	G	H	I	J	K	L	M
		TIME *		0726	1604	1610	0643	1635	1555	0634	1441	0659	1611	1606	0639	1626
		DAY		1	1	3	5	5	7	10	10	12	12	14	17	17
		DATE		1-25	1-25	1-27	1-29	1-29	1-31	2-3	2-3	2-5	2-5	2-7	2-10	2-10
		NAME		Plasma Iodine, Micrograms/100 ml												
A	1	Thi	No Bursoline Salted Water Only	< 10	< 10	< 10	< 10	< 10	< 10	< 10	< 10	< 10	< 10	< 10	< 10	< 10
	2	Bur		< 10	< 10	< 10	< 10	< 10	< 10	< 10	No Sample				< 10	< 10
	3	Men		< 10	< 10	< 10	< 10	< 10	< 10	< 10	< 10	< 10	< 10	< 10	< 10	< 10
	4	Del		< 10	< 10	< 10	< 10	< 10	< 10	< 10	< 10	< 10	< 10	< 10	< 10	< 10
		AVERAGE		< 10	< 10	< 10	< 10	< 10	< 10	< 10	< 10	< 10	< 10	< 10	< 10	< 10
B	5	Fle	On Bursoline 0700 25 January	< 10	155	345	65	480	560	230	465	200	405	730	830	1320
	6	Sce		10	65	175	60	240	260	125	305	15	245	75	165	345
	7	Pul		< 10	35	280	55	365	485	200	625	105	225	710	380	925
	8	Tho		< 10	135	310	140	290	390	85	325	90	340	455	225	580
	9	Dev		< 10	185	455	95	500	620	230	565	125	630	760	520	950
	10	Mag		< 10	115	290	30	465	450	115	480	50	520	675	240	875
	11	Lue		< 10	55	240	40	455	425	200	465	85	430	495	265	585
	12	Oli		< 10	95	570	125	655	500	215	300	105	560	800	140	860
	13	Kel		< 10	135	305	105	455	585	310	490	120	625	615	435	675
	14	Pem		< 10	75	260	45	260	185	125	340	30	360	365	195	590
		AVERAGE		< 10	105	323	76	417	446	184	436	93	434	568	370	771

* Bleeding started at the noted time; 10 to 20 minutes were required to bleed the group.

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TABLE 4 SHEET 2

SUMMARY OF PLASMA IODINE CONCENTRATIONS

GROUP	SUBJECT NO.	BLEEDING	N	O	P	Q	R	S	T	U	V	W	X	Y	Z	A¹	B¹
		TIME	0657	1558	1603	0633	1624	0636	1613	1606	0642	1612	0636	1623	1603	0644	1604
		DAY	19	19	21	24	24	26	26	28	31	31	33	33	35	38	38
		DATE	2-12	2-12	2-14	2-17	2-17	2-19	2-19	2-21	2-24	2-24	2-26	2-26	2-28	3-3	3-3
		NAME	Plasma Iodine, Micrograms/100 ml														
A	1	Thi	< 10	< 10	< 10	<10	< 10	<10	< 10	< 10	< 10	< 10	<10	< 10	< 10	< 10	< 10
	2	Bur	< 10	< 10	< 10	<10	<10	<10	< 10	< 10	< 10	< 10	<10	< 10	< 10	< 10	< 10
	3	Man	< 10	< 10	< 10	<10	<10	<10	< 10	< 10	< 10	< 10	<10	-	-	< 10	-
	4	Del	< 10	< 10	< 10	<10	< 10	<10	< 10	< 10	< 10	< 10	<10	< 10	< 10	< 10	< 10
		AVERAGE	< 10	< 10	< 10	<10	< 10	<10	< 10	< 10	< 10	< 10	<10	< 10	< 10	< 10	< 10
B	5	Fie	200	855	800	950	1160	245	610	1550	575	900	175	960	1840	1020	1760
	6	Sce	115	375	435	235	625	125	680	860	390	1020	190	865	960	480	1060
	7	Pul	85	975	800	370	690	70	675	1110	320	745	85	755	1310	695	1290
	8	Tho	100	600	675	300	805	55	625	990	160	625	35	590	910	510	1090
	9	Dev	165	785	960	485	1050	No Sample	935	1480	550	1090	145	910	1480	815	1530
	10	Mag	20	720	800	250	835	175	900	1340	160	1100	35	870	1420	600	1380
	11	Luc	55	455	640	80	205	10	525	750	220	595	50	575	725	270	800
	12	Oli	110	845	1270	305	1200	140	980	1790	830	1210	125	900	1940	1010	1510
	13	Kel	90	665	930	370	1090	210	1120	1700	400	1220	165	1140	1710	1140	1560
	14	Pum	35	465	510	235	610	55	580	885	135	580	20	565	800	320	840
		AVERAGE	98	674	782	388	827	121	763	1246	374	909	103	813	1310	686	1282

TABLE 4 SHEET 3

SUMMARY OF PLASMA IODINE CONCENTRATIONS

GROUP	SUBJECT NO.	BLEEDING		C^1	D^1	E^1	F^1	G^1	H^1	I^1	J^1		K^1	L^1	M^1	N^1
		TIME		0814	0636	1601	0743	1630	0631	0639	1650		0811	0733	0657	0749
		DAY		39	40	40	41	42	43	45	45		46	47	48	49
		DATE		3-4	3-5	3-5	3-6	3-7	3-8	3-10	3-10		3-11	3-12	3-13	3-14
		NAME	Plasma Iodine, Micrograms/100 ml													
A	1	Thi	ON BURSOLINE 0700 5 March	-	< 10	1260	-	1550	-	445	1160	OFF BURSOLINE 0700 11 March	380	50	35	< 10
	2	Bur		-	< 10	1040	-	1400	-	510	1240		445	100	25	< 10
	3	Men		-	-	-	-	-	-	-	-		-	-	-	< 10
	4	Del		-	< 10	760	-	1080	-	405	960		370	40	10	< 10
		AVERAGE		-	< 10	1020	-	1343	-	453	1120		398	63	23	< 10
B	5	Fie	OFF BURSOLINE 0700 4 March	640	100	-	20	-	< 10	< 10	-		-	-	-	< 10
	6	Sce		320	50	-	15	-	< 10	< 10	-		-	-	-	< 10
	7	Pul		450	55	-	15	-	< 10	< 10	-		-	-	-	< 10
	8	Tho		245	25	-	< 10	-	< 10	< 10	-		-	-	-	< 10
	9	Dev		510	110	-	30	-	< 10	< 10	-		-	-	-	< 10
	10	Mag		275	25	-	< 10	-	< 10	< 10	-		-	-	-	< 10
	11	Lue		180	30	-	< 10	-	< 10	< 10	-		-	-	-	< 10
	12	Oli		510	75	-	35	-	20	< 10	-		-	-	-	< 10
	13	Kel		540	95	-	15	-	< 10	< 10	-		-	-	-	< 10
	14	Pem		180	25	-	< 10	-	< 10	< 10	-		-	-	-	< 10
		AVERAGE		385	59	-	13	-	< 10	< 10	-		-	-	-	< 10

TABLE 5

Iodine Intake and Urine Excretion for All Subjects by Periods of One Week

Group B Received Bursoline Day 1 through Day 38, Group A Day 40 through Day 45

Week	Exp. Day	Subj.	Group B											Group A			
			Fie	Sce	Pul	Tho	Dev	Mag	Lue	Oli	Kel	Pem	Average	Thi	Bur	Del	Average
		No.	5	6	7	8	9	10	11	12	13	14		1	2	4	
1	1 thru 4	I*	330	207	253	307	457	309	243	273	350	421	324	--	--	--	--
		O	253	157	93	176	323	153	165	212	257	267	213	--	--	--	--
		%	77	76	37	57	71	50	68	78	73	63	65	--	--	--	--
2	5 thru 11	I	700	494	992	550	895	765	569	908	1160	710	804	--	--	--	--
		O	623	431	848	450	690	814	510	907	1046	459	691	--	--	--	--
		%	89	87	85	82	77	107	90	100	90	65	86	--	--	--	--
3	12 thru 18	I	1043	588	1492	932	1263	1410	933	1462	1426	1142	1169	--	--	--	--
		O	931	588	1338	829	902	1149	669	1035	1302	1020	976	--	--	--	--
		%	89	100	90	89	71	81	72	71	91	89	83	--	--	--	--
4	19 thru 25	I	1245	1046	1540	1231	1348	1595	791	2043	2144	1402	1439	--	--	--	--
		O	1056	1012	989	990	883	1230	523	1428	1668	1074	1085	--	--	--	--
		%	85	97	64	80	65	77	66	70	78	77	75	--	--	--	--
5	26 thru 32	I	1362	1675	1445	1225	1623	1679	1063	2060	2367	1712	1621	--	--	--	--
		O	1027	1475	756	1008	1197	1125	790	1297	1797	1096	1157	--	--	--	--
		%	75	88	52	82	74	67	74	63	76	64	71	--	--	--	--
6	33 thru 39	I	1654	1668	1592	1454	1874	1937	1240	2121	2436	1881	1786	--	--	--	--
		O	970	1292	1005	1117	884	1222	662	1298	1751	1171	1137	--	--	--	--
		%	59	77	63	77	47	63	53	61	72	62	64	--	--	--	--
7	40 thru 46	I	0	0	0	0	0	0	0	0	0	0	0	2674	2103	1888	2222
		O	28	29	36	39	25	9	7	19	27	17	24	1933	1555	1399	1629
		%	--	--	--	--	--	--	--	--	--	--	--	72	74	74	73
8	47 thru 48	I	--	--	--	--	--	--	--	--	--	--	--	0	0	0	0
		O	--	--	--	--	--	--	--	--	--	--	--	11	27.	24	21
		%	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--
	B 1-46 / A 40-48	I	6332	5677	7313	5699	7460	7695	4837	8868	9883	7268	7143	2674	2103	1888	2222
		O	4888	4984	5065	4609	4904	5702	3326	6196	7848	5104	5283	1944	1582	1423	1650
		%	77	88	69	81	66	74	69	70	79	70	74	73	75	75	74

* I - Intake for the period, mgm.
O - Output in the urine for the period, mgm.
% - Percent of the intake recovered in the urine for the period.

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TABLE 6

SUMMARY OF SWEAT COLLECTION DATA

Exp. Day	Sub-ject	Method of Collection	Time (Midpoint) Hrs.	Collection Interval (Min.)		Sweat Loss g/hr.*		Iodine Concentration Micrograms/100 ml.	
				Total	Walk	Total	Unevaporated	Plasma (Interpolated)	Sweat*
20	Thi	Suit	1045	38	30	1530	1170	-	0
"	Tho	"	1034	38	30	1790	1510	-	258
22	Thi	"	1426	38	30	1660	1440	-	0
"	Tho	"	1415	38	30	1480	1320	-	211
23	Ful	"	1536	37	30	911	750	-	366
"	Tho	"	1543	37	30	1540	1410	-	316
24	Ful	"	1016	36	30	1700	1240	-	280
"	Tho	"	1024	38	30	1830	1560	-	206
26	Ful	"	1033	76	60	1480	1290	380	196
"	Ful	"	1508	79	60	905	760	505	306
"	Tho	"	1042	77	60	1820	1530	245	110
"	Tho	"	1516	76	60	1330	1090	585	319
28	Dev	"	1042	77	60	1870	1520	1040	331
"	Dev	"	1511	69	50	1520	1280	1400	398
"	Pem	"	1030	73	60	1850	1570	520	223
"	Pem	"	1459	64	50	1720	1430	790	210
38	Oli	Sleeve	1438	62	62	-	257	1500	658
"	Sce	"	1443	60	60	-	147	870	326
43	Bur	"	1510	15	15	-	96	-	367
"	Del	"	1508	16	16	-	113	-	295

* Sweat iodine concentration calculated on the total weight loss uncorrected for CO_2 excess or respiratory tract evaporation.

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TABLE 7

IODINE CONCENTRATION IN SWEAT FROM THE WHOLE MAN AND FROM THE ARM

Exp. Day	Subject	Method of Collection	Time (Midpoint)	Collection Interval (Min.)		Sweat Loss * g/hr.		Iodine Concentration Micrograms/100 ml.	
				Total	Walk	Total	Unevapor-ated	Plasma (Interpolated)	Sweat*
45	Bur	Suit	1013	40	30	1880	1530	850	281
"	Bur	Sleeve	1047	15	15	-	208	910	394
"	Bur	Suit	1525	42	30	1660	1480	1240	398
"	Bur	Sleeve	1559	15	15	-	208	1620	475
"	Del	Suit	1022	38	30	2480	2150	680	223
"	Del	Sleeve	1054	15	15	-	220	720	295
"	Del	Suit	1535	39	30	2480	2010	880	237
"	Del	Sleeve	1607	15	15	-	188	900	305

* Sweat iodine concentration calculated on the total weight loss uncorrected for CO_2 excess or respiratory tract evaporation.

TABLE 7

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TABLE 8

APPROXIMATE IODINE BALANCE
See Text for Methods of Estimation

SUBJECT	WEEK*	IODINE BALANCE IN	OUT URINE		SWEAT		FECES		TOTAL	
		Mgm	Mgm	%	Mgm	%	Mgm	%	Mgm	%
SCE	2	494	431	87.3	11	2.3	1.7	0.35	444	89.9
	5	1675	1475	88.0	69	4.1	5.9	0.35	1550	92.5
	All	5677	4984	87.8	215	3.8	19.9	0.35	5218	91.9
THO	2	550	450	81.8	17	3.0	1.9	0.35	469	85.1
	5	1225	1008	82.3	79	6.5	4.3	0.35	1092	89.1
	All	5699	4609	80.9	337	5.9	20.0	0.35	4966	87.1
DEV	2	895	690	77.1	37	4.2	3.1	0.35	730	81.6
	5	1623	1197	73.8	153	9.4	5.7	0.35	1356	83.5
	All	7460	4904	65.7	575	7.7	26.1	0.35	5504	73.8
GROUP B (10 Men)	2	804	691	85.9	24	3.0	2.8	0.35	718	89.3
	5	1621	1157	71.4	117	7.2	5.7	0.35	1280	78.9
	All	7143	5283	73.9	430	6.0	25.0	0.35	5738	80.3

* Correspond to same intervals as in Table 5

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TABLE 9

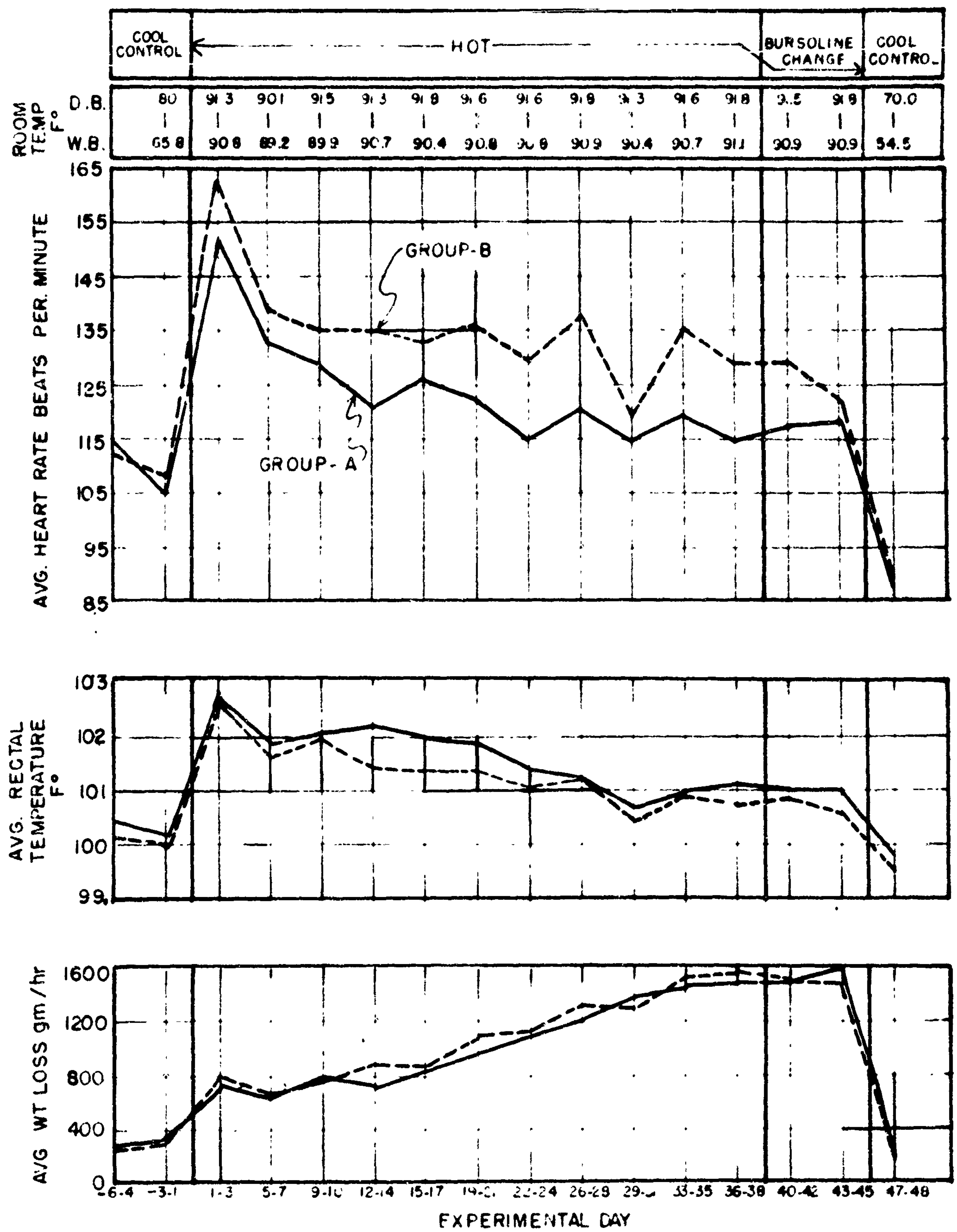
RECOVERIES OF KI ADDED TO PLASMA, PLASMA FILTRATE, URINE AND WATER

KI Added to	No. of Experi-ments	MICROGRAMS IODINE			Per Cent Iodine Recovered
		Added	Determined		
			Avg.	S.D.	
		PER 100 ml. PLASMA			
Plasma Before Precipitation	2	751	713	-	95
	4	471	445	-	95
	4	377	384	-	102
	2	285	266	-	93
	2	95	95	-	100
	2	7.5	8.5	-	113
Plasma Filtrate 20 ml.	89	380	366	± 8.4	96
	35	76	73	± 5.1	96
	20	19	20	± 3.4	105
	20	9.5	10.4	± 1.9	110
		PER SAMPLE			
Urine .02 ml.	31	1.90	1.85	± 0.089	97
.01 ml.	10	0.95	0.97	± 0.045	102
.2 ml.	22	0.76	0.70	± 0.123	92
.1 ml.	8	0.38	0.31	± 0.019	82
Water	35	3.80	3.98	± 0.15	105

TABLE 9

Incl. #4

HEART RATE RECTAL TEMPERATURE, AND HOURLY WEIGHT LOSS BY 3-DAY PERIODS



Incl. #5

CHART-1

BASAL METABOLIC RATE

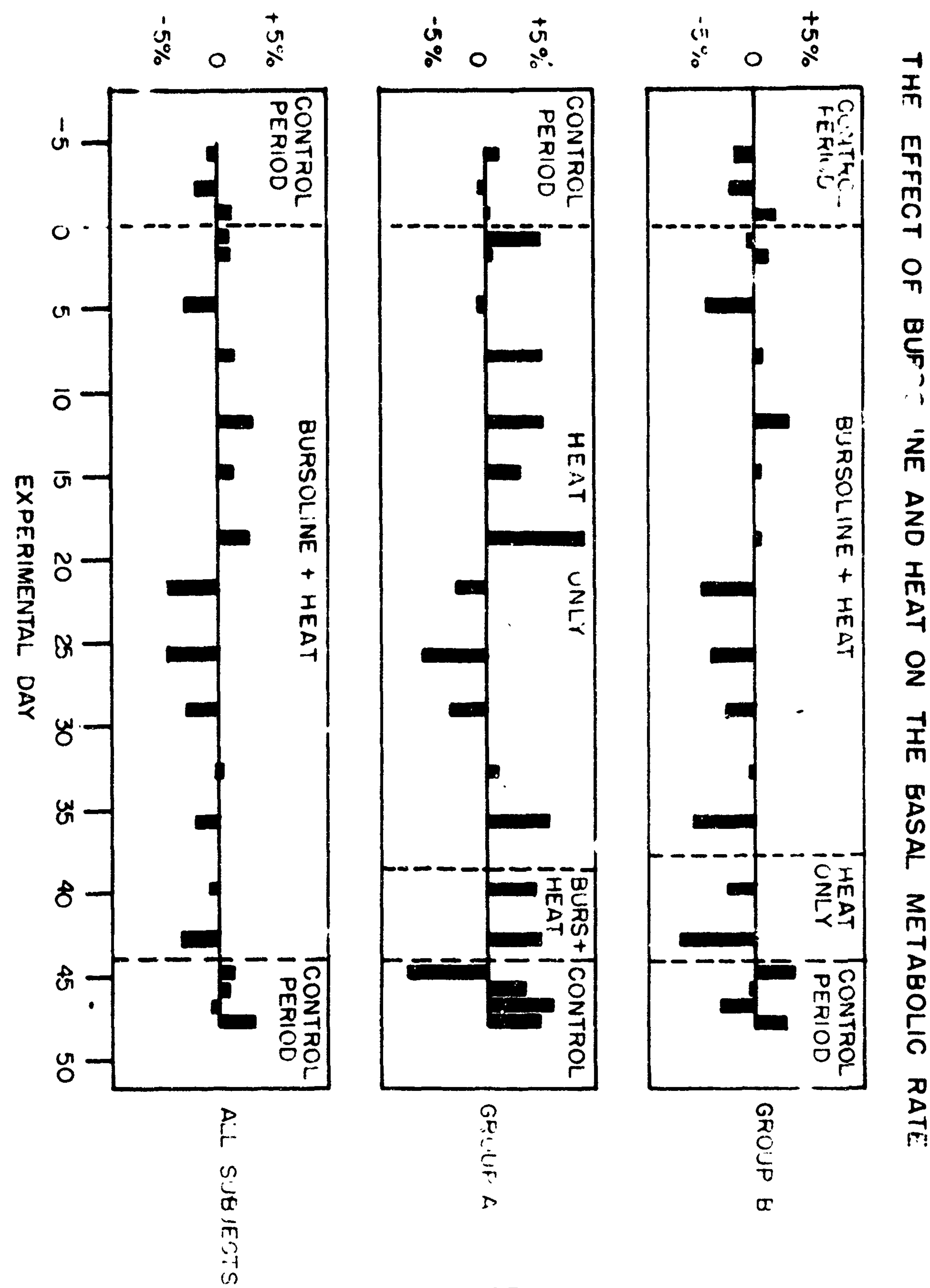
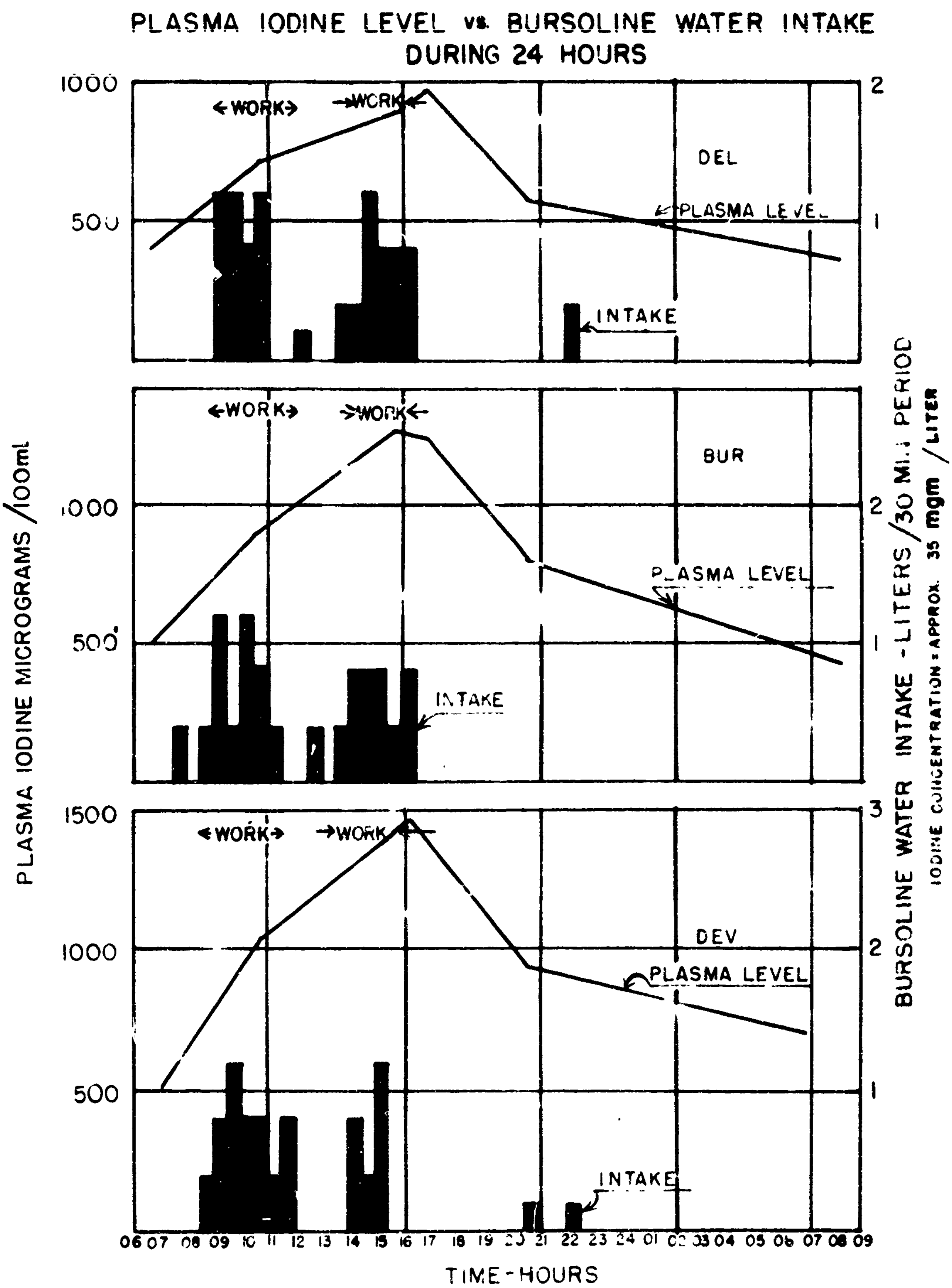


CHART-2

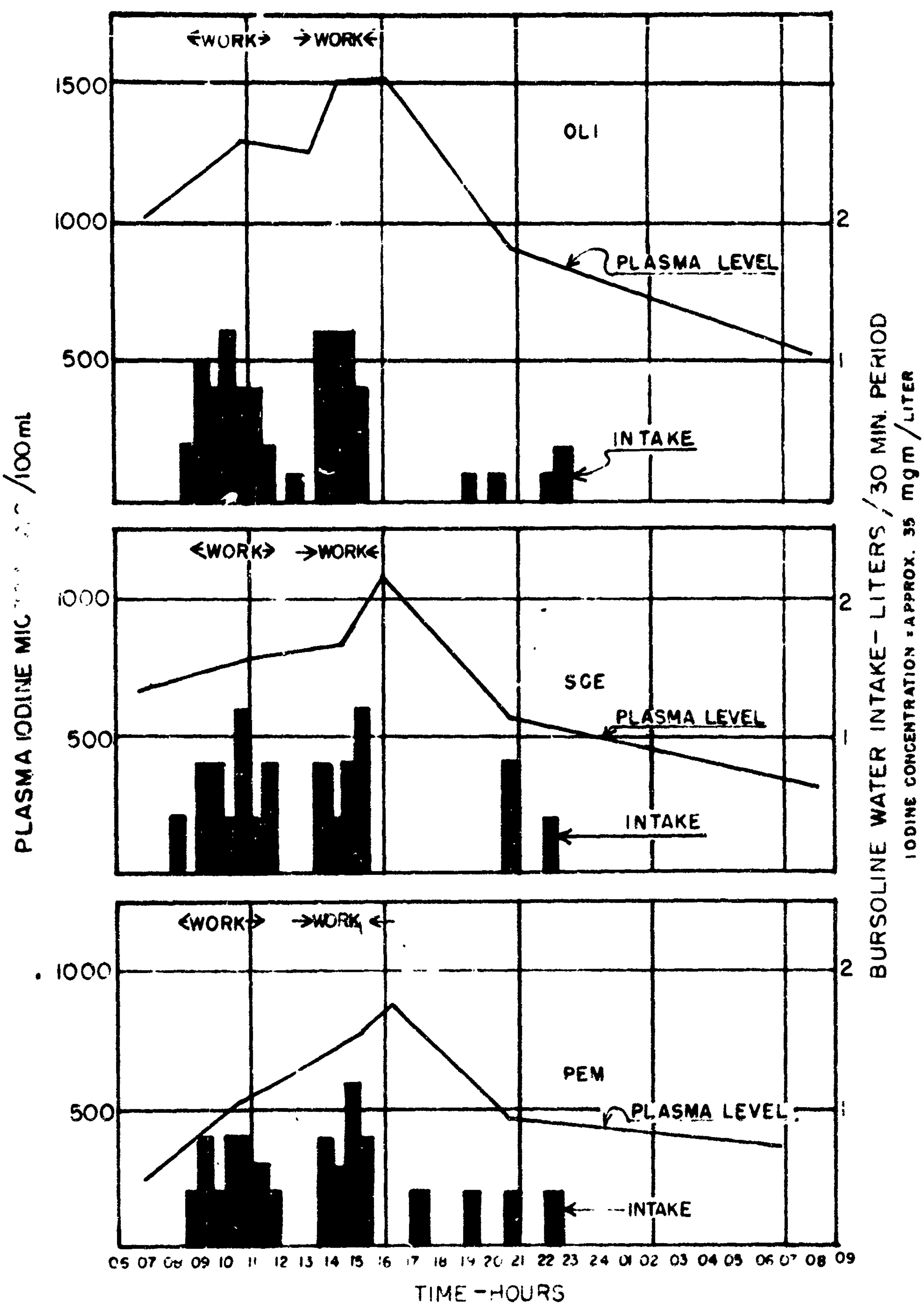
CHART 2



Incl. #5

CHART 3a

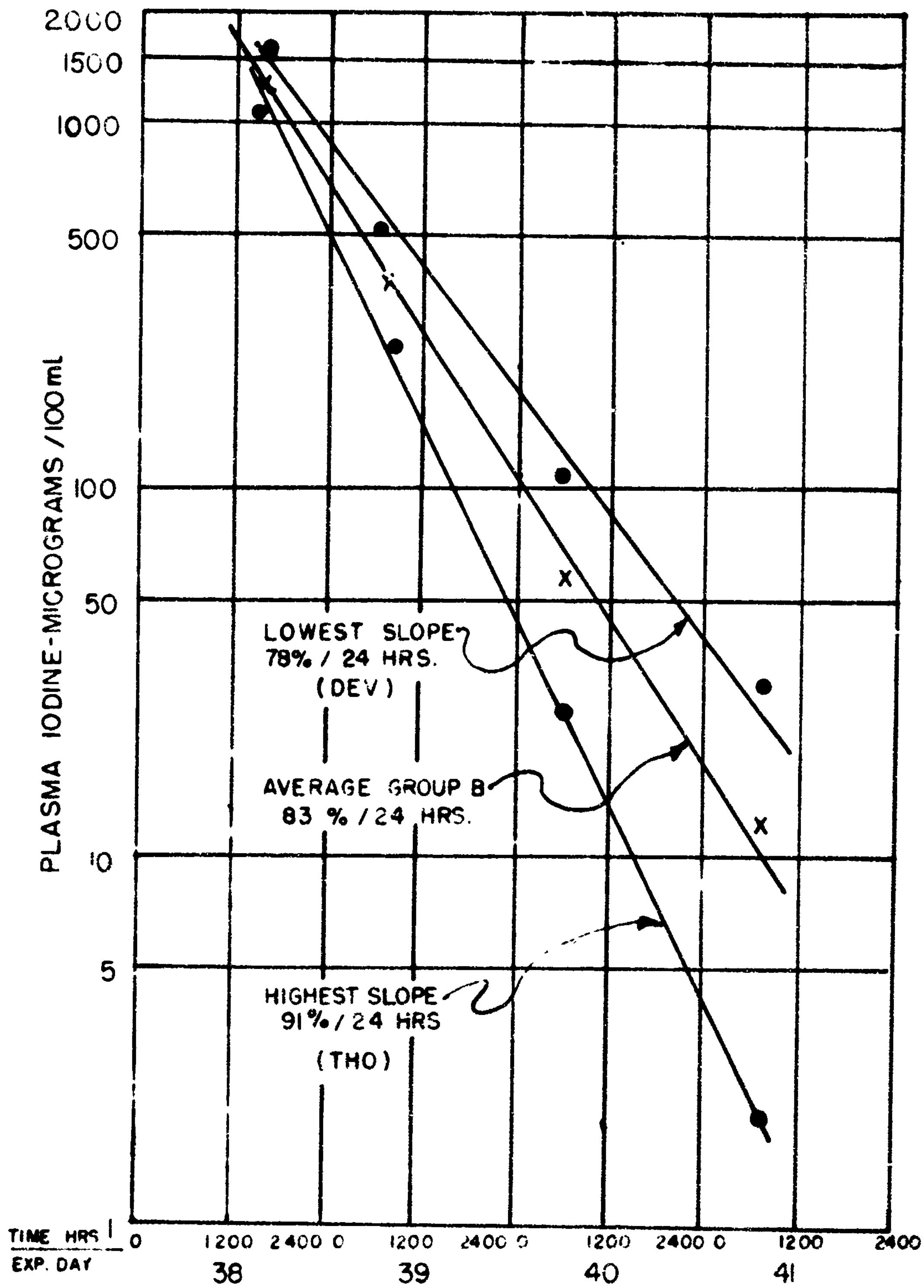
PLASMA IODI _ LEVEL vs BURSOLINE WAT R INTAKE
DURING 24 HOURS



Incl. 5

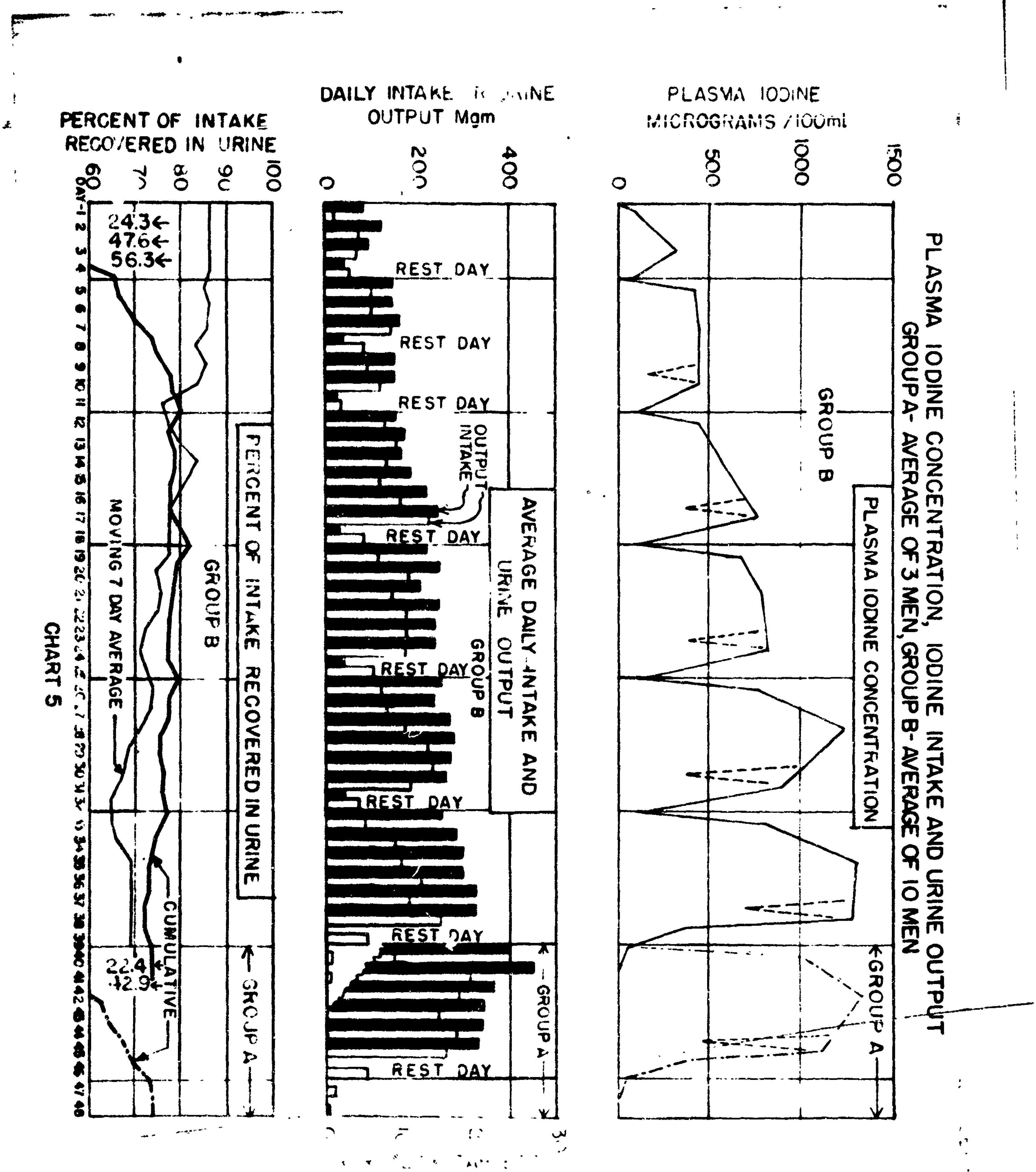
CHART 3 b

RATE OF DISAPPEARANCE OF IODINE FROM PLASMA
AFTER DISCONTINUING BURSOLINE
GROUP B



Incl. #5

CHART- 4



Incl. #5

CHART 5

RELATIONSHIP BETWEEN IODINE INTAKE AND PLASMA IODINE CONCENTRATION. GROUP B

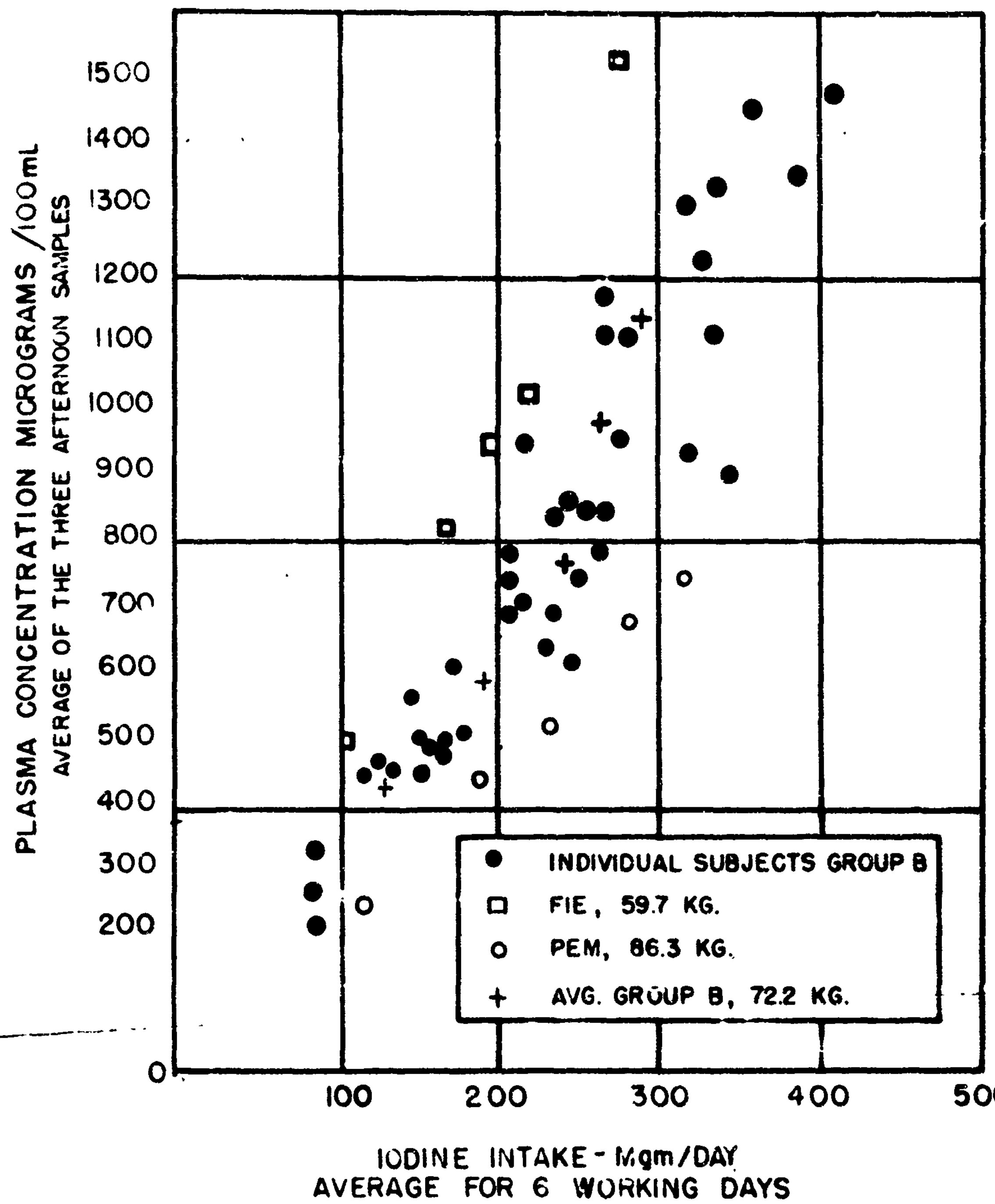


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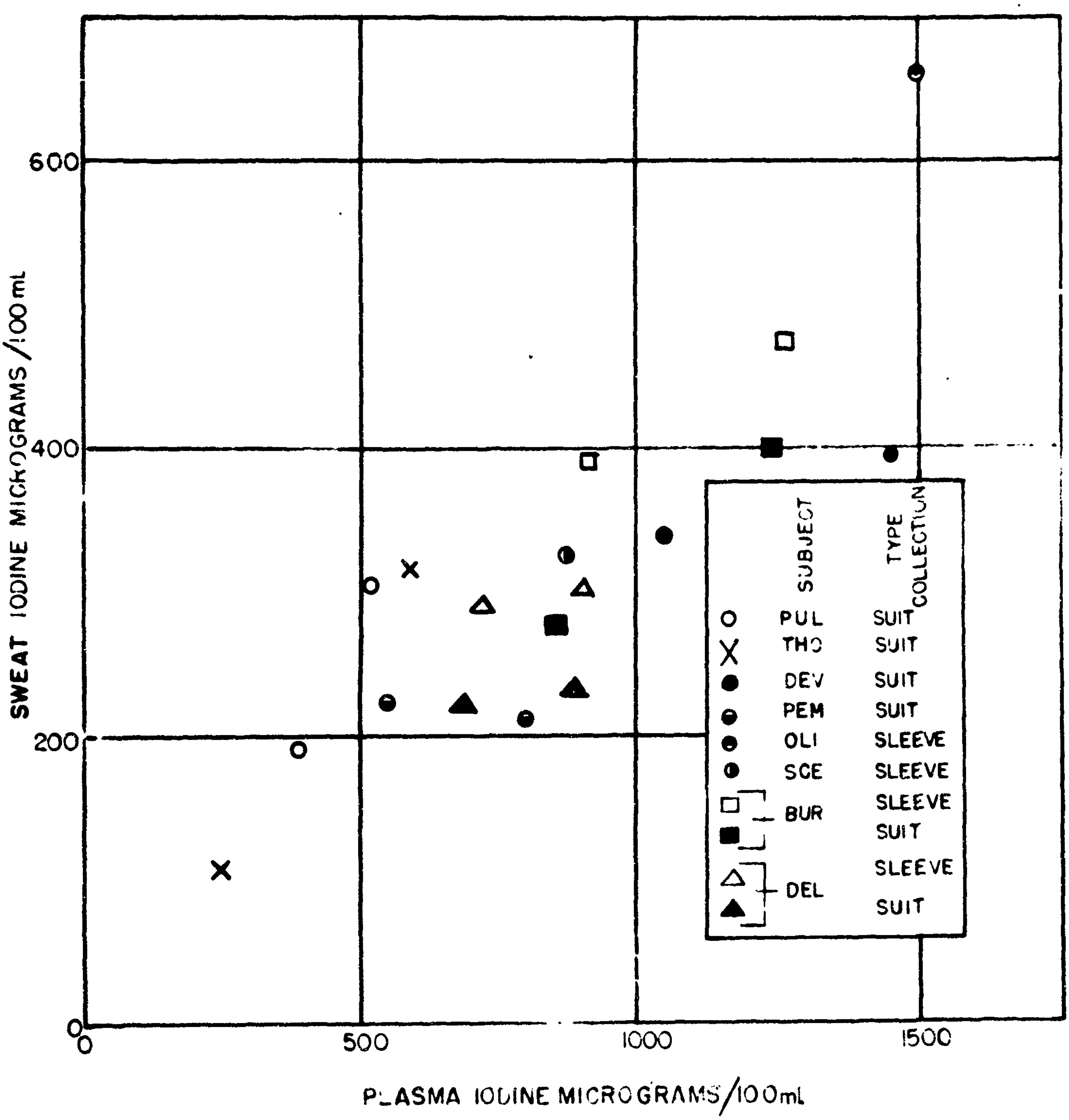
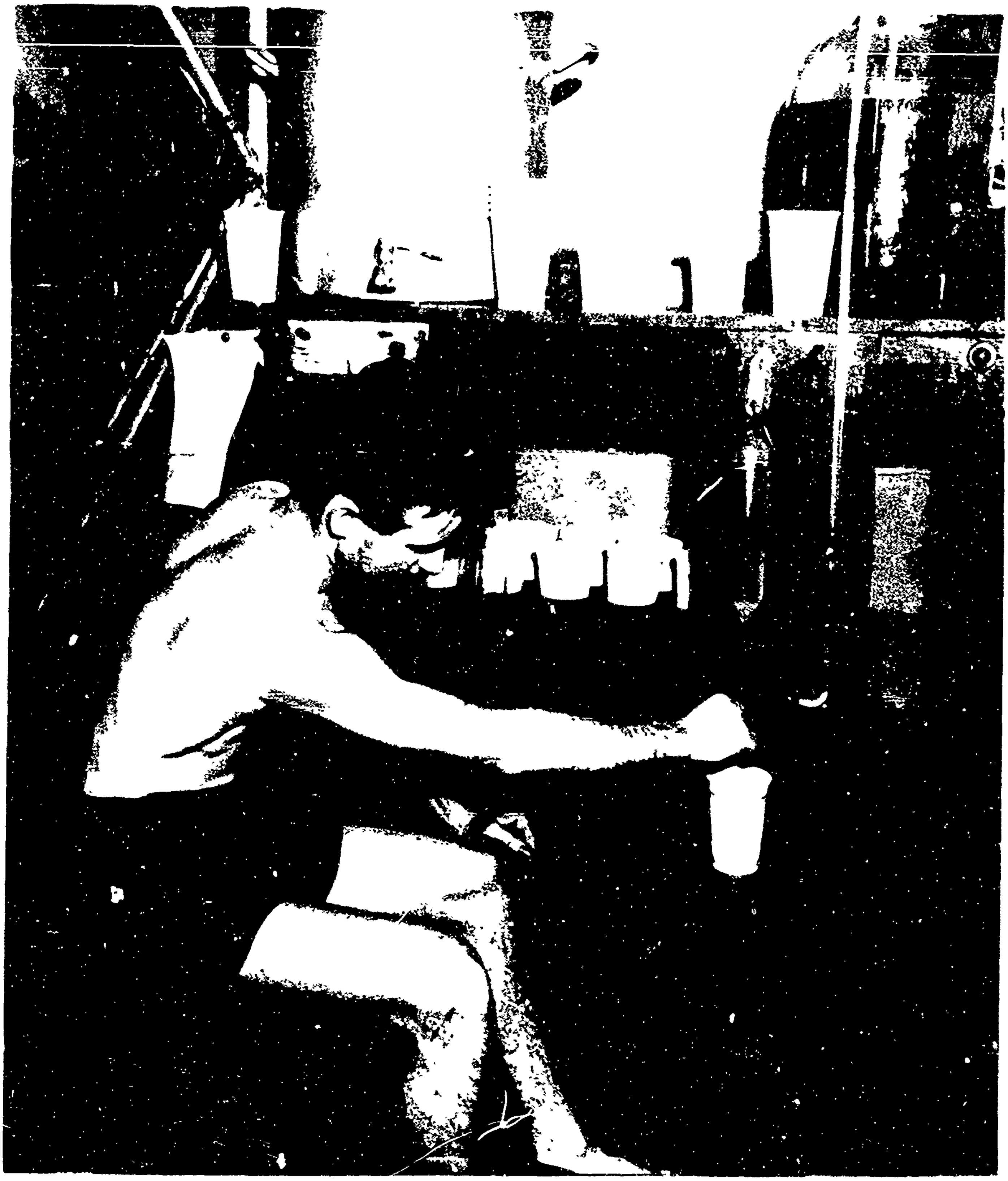
CHART 6

CONCENTRATION OF IODINE IN SWEAT AS A FUNCTION OF PLASMA IODINE CONCENTRATION



Incl. #5

CHART-7



FIXED VOLUME WATER DISPENSER
ARMORED MEDICAL RESEARCH LABORATORY
FORT KNOX, KY.
Project No. 50 Figure 1

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